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REVIEW ARTICLE

The TURis System for Transurethral Resection of the Prostate: A NICE Medical Technology Guidance

Andrew Cleves[1] · Paul Dimmock[2] · Neil Hewitt[2] · Grace Carolan-Rees[1]

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Abstract The transurethral resection in saline (TURis) system was notified by the company Olympus Medical to the National Institute of Health and Care Excellence's (NICE's) Medical Technologies Evaluation Programme. Following selection for medical technologies guidance, the company developed a submission of clinical and economic evidence for evaluation. TURis is a bipolar surgical system for treating men with lower urinary tract symptoms due to benign prostatic enlargement. The comparator is any monopolar transurethral resection of the prostate (mTURP) system. Cedar, a collaboration between Cardiff and Vale University Health Board, Cardiff University and Swansea University in the UK, acted as an External Assessment Centre (EAC) for NICE to independently critique the company's submission of evidence. Eight randomised trials provided evidence for TURis, demonstrating efficacy equivalent to that of mTURP for improvement of symptoms. The company presented meta-analyses of key outcome measures, and the EAC made methodological modifications in response to the heterogeneity of the trial data. The EAC analysis found that TURis substantially reduced the relative risks of transurethral resection syndrome (relative risk 0.18 [95 % confidence interval 0.05–0.62]) and blood transfusion (relative risk 0.35 [95 % confidence interval 0.19–0.65]). The company provided a de novo economic model comparing TURis with mTURP. The EAC critiqued the model methodology and made modifications. This found TURis to be cost saving at £70.55 per case for existing Olympus customers and cost incurring at £19.80 per case for non-Olympus customers. When an additional scenario based on the only available data on readmission (due to any cause) from a single trial was modelled, the estimated cost saving per case was £375.02 for existing users of Olympus electrosurgery equipment and £284.66 per case when new Olympus equipment would need to be purchased. Meta-analysis of eight randomised trials showed that TURis is associated with a statistically significantly reduced risk of transurethral resection syndrome and a reduced need for blood transfusion—two factors that may drive cost saving for the National Health Service. The clinical data are equivocal as to whether TURis shortens the hospital stay. Limited data from a single study suggest that TURis may reduce the rate of readmission after surgery. The NICE guidance supports adoption of the TURis technology for performing transurethral resection of the prostate in men with lower urinary tract symptoms due to benign prostatic enlargement.

✉ Andrew Cleves
andrew.cleves@wales.nhs.uk

[1] Cedar, Cardiff and Vale University Health Board, Cardiff Medicentre, Heath Park Campus, Cardiff CF14 4UJ, UK

[2] National Institute for Health and Care Excellence, Manchester, UK

Key Points for Decision Makers

The efficacy of transurethral resection in saline (TURis) is equivalent to that of monopolar transurethral resection of the prostate (mTURP) in terms of improving lower urinary tract symptoms due to benign prostatic enlargement.

TURis is associated with a reduced risk of transurethral resection syndrome and reduced need for blood transfusion in comparison with mTURP.

The clinical data are equivocal as to whether TURis shortens the hospital stay in comparison with mTURP.

The TURis system is likely to be cost saving for hospitals that already buy mTURP consumables from Olympus at the list price. TURis may incur a cost for non-Olympus customers.

Data from one randomised study suggest that TURis may substantially reduce the rate of readmission (due to any cause) following surgery in comparison with mTURP.

Clinical experts suggest that most hospitals replacing their capital equipment for transurethral resection of the prostate would opt for a bipolar system rather than a monopolar system.

1 Introduction

The National Institute for Health and Care Excellence (NICE) provides the Medical Technologies Evaluation Programme (MTEP). MTEP provides guidance on medical devices and diagnostic technologies to the National Health Service (NHS) in England and supports the adoption of technologies that improve clinical outcomes or the patient experience and/or that result in cost savings [1]. The process followed in MTEP is explained in the first publication in this series [1]. This article summarises the External Assessment Centre (EAC) report [2] and how it was used to inform the NICE Medical Technology Guidance on the transurethral resection in saline (TURis) system for transurethral resection of the prostate (TURP) [3]. Cedar, the EAC for this guidance, is a collaboration between Cardiff and Vale University Health Board, Cardiff University and Swansea University.

Olympus Medical, the company supplying TURis, notified the technology to NICE.

2 Background to the Conditions and the Device

In May 2010, NICE published a clinical guideline (NICE CG97) on lower urinary tract symptoms (LUTS), defining LUTS as storage, voiding and post-micturition symptoms affecting the lower urinary tract [4]. In men, the most common cause is benign prostatic enlargement (BPE). Age is an important risk factor for LUTS, and the prevalence of LUTS increases as men get older. Bothersome LUTS can occur in up to 30 % of men older than 65 years, who represent a large group potentially requiring treatment [4].

Men with LUTS due to BPE may be managed by watchful waiting if their symptoms are mild or moderate. For bothersome symptoms, education and lifestyle advice, or medical therapies are usually the first-line treatments. Medical therapies include muscarinic receptor antagonists, 5-alpha-reductase inhibitors, alpha-1 blockers and vasopressin analogues [5].

NICE CG97 recommends that clinicians should offer surgery only if voiding symptoms are severe or if drug treatment and conservative management options have been unsuccessful or are not appropriate [4]. Patient choice, prostate volume, anaesthetic risk, anticoagulant therapy and the local availability of different surgical techniques are relevant factors when surgery is considered for a patient with LUTS [5]. TURP has been performed to treat LUTS since the 1930s [6, 7] and is less invasive than open prostatectomy. Despite the relatively recent emergence of other surgical therapies, which include transurethral incision or stent, laser enucleation or vaporisation and microwave ablation, TURP remains the mainstay surgical technique to treat LUTS due to BPE [5]. While some surgical treatments have restricted suitability according to prostate size, TURP is a surgical treatment option for men with all prostate sizes [4].

3 Decision Problem (Scope)

3.1 Population

The relevant population is adult men with LUTS presumed secondary to BPE, in whom surgical intervention, most commonly monopolar transurethral resection of the prostate (mTURP), is indicated [8].

3.2 Comparator (Current Practice)

Standard TURP is a monopolar electrosurgical technique (mTURP). The surgeon introduces a resectoscope through the urethra, and a generator generates an electrical current,

which is delivered to an active loop electrode or roller electrode at the end of the resectoscope. The electrode focuses current on the prostate tissue, enabling the surgeon to cut away chips of tissue or coagulate bleeding blood vessels. The current disperses through the patient's body and returns to the generator via a return electrode, which is a conductive, adhesive pad, usually placed on the patient's thigh. The return electrode requires careful attention because if it is not correctly adhered, burn injuries may result [9]. Also, mTURP requires a non-conductive irrigation fluid to wash away the tissue chips and blood, examples being solutions of glycine, mannitol or sorbitol. These solutions are not isotonic with blood and may be absorbed by the body during surgery. Fluid absorption may lead to a rare but potentially serious condition called transurethral resection (TUR) syndrome, characterised by fluid overload and hyponatraemia. The incidence of TUR syndrome is 0.5–8 %, with a reported mortality rate of 0.2–0.8 % [10].

Following surgery, the patient has a urinary catheter and undergoes bladder irrigation for a few days to clear debris and blood. Standard practice is to discharge patients when the catheter is removed and the patient can pass urine satisfactorily.

The scope for MTG23 states that any mTURP system may be a comparator for TURis [8].

3.3 Intervention (the TURis System)

TURis is a bipolar system used to perform TURP and may be used in the same patient group who undergo mTURP. 'Bipolar' means that the active and return electrodes are both located within the resectoscope. Therefore, electrical current is focused on the prostate tissue but does not disperse through the patient's body, and no externally placed return electrode is required. In addition, there is no need for a non-conductive irrigation fluid, and normal saline may be used. Saline is nearly isotonic with blood, and the company has claimed that a benefit of TURis is that the risk of TUR syndrome is eliminated. Other claimed benefits include improved coagulation during surgery, reduced surgical blood loss and better visibility for the surgeon. TURis uses higher generator energy settings than mTURP. Other bipolar technologies exist but are outside of the guidance scope [8].

3.4 Outcomes

The outcomes studied in the evaluation of TURis were:

- Incidence of TUR syndrome.
- Incidence of blood transfusion.
- Incidence of clot retention.
- Length of hospital stay.
- Time to catheter removal.
- Procedure time.
- Incidence of readmission due to haemorrhage.
- Incidence of urethral stricture and bladder neck contracture.
- Incidence of repeat procedures due to incomplete resection.

4 Review of Clinical and Economic Evidence

4.1 Clinical Effectiveness Evidence

4.1.1 Company's Review of Clinical Effectiveness Evidence

The company undertook a comprehensive literature search, which identified a relatively large volume of evidence within the scope, restricted to English-language papers and English-language abstracts, as per MTEP procedure. The company included 16 publications presenting data from randomised studies comparing TURis with mTURP [6, 11–25]. Of these, four publications were conference abstracts from a single study [16–19] and two were Spanish-language [11] or German-language [25] full papers with English-language abstracts.

The company also included publications from observational studies [26–33]. Of these, three were full papers [29, 31, 33] and five were conference abstracts [26–28, 30, 32]. All but two observational studies [27, 29] had a comparator for TURis, most often mTURP, but sometimes including other surgical procedures.

The company undertook meta-analyses of randomised trials (TURis versus mTURP) to present the clinical evidence relevant to TURis and did not place great emphasis on the data from the observational studies. The company included a meta-analysis of clot retention, an outcome not specified in the scope [8].

4.1.2 Critique of Company's Clinical Evidence Submission

The EAC performed an independent literature search and identified all of the evidence provided by the company, plus three additional studies published as full papers: two randomised trials comparing TURis with mTURP [34, 35] and one observational study of TURis [36]. The EAC agreed with the company's focus on meta-analysis of randomised studies and, having also reviewed data from the observational studies, concluded that these did not significantly add to the evaluation of TURis. The EAC considered that eight randomised trials (published as 13

papers [6, 12–15, 20–25, 34, 35]) were eligible for inclusion in its analysis. Table 1 presents the characteristics and published papers of each randomised study included in the analysis by the EAC, and Table 2 presents the studies excluded by the EAC.

The eight randomised trials (Table 1) all presented data on the patient group and the comparison specified in the scope. None of the studies were undertaken in the UK. Most studies were similar in terms of baseline prostate size, which ranged typically from 45 to 60 g. The first of two studies from the same team in China had the largest baseline prostate size of 78 g [13]. This study also had the longest procedure times for both TURis (88 min) and mTURP (105 min) [13], whereas most of the other studies had average procedure times of <60 min.

The study sample sizes ranged from 40 to 550 subjects. Many studies did not define a primary outcome measure. Only three studies stated that patients were blinded to treatment allocation [13, 14, 34]. Only one study stated that assessors of outcome were blinded to allocation status and that a sample size calculation was performed [34]. It is therefore unknown whether most of the studies had adequate statistical power to detect important differences in many of the outcome measures. Five studies reported the method used to randomly allocate subjects to treatment [6, 14, 15, 20, 21, 23, 29, 34]. No study reported that an intention-to-treat analysis was performed. Therefore, the eight included randomised trials [6, 12–15, 20–25, 34, 35] carried some risk of bias but represented a substantial volume of evidence of reasonable quality to inform the evaluation.

Table 3 summarises the results of the company's meta-analyses. The company's analysis did not demonstrate that TURis statistically significantly reduced the risk of TUR syndrome (relative risk [RR] 0.28 [95 % confidence interval (CI) 0.08–1.02]) or clot retention (RR 0.63 [95 % CI 0.21–1.90]), though the risk of blood transfusion was substantially reduced by TURis (RR 0.36 [95 % CI 0.16–0.80]). The company found that TURis did not significantly shorten the procedure time (mean difference −1.68 [95 % CI −4.18–0.8]) minutes) but concluded that TURis shortened the time to catheter removal (mean difference −0.23 [95 % CI −0.38 to −0.08] days) and also the hospital stay (mean difference −0.52 [95 % CI −0.74 to −0.30] days).

4.1.3 Additional Work Carried Out by the External Assessment Centre

The EAC studied the methodology of the company's meta-analysis and reproduced the analyses with checks or modifications as follows:

- Adding data from additional randomised trials identified by the EAC [34, 35].
- Removing data that were duplicated in the company's analysis, because of repeat publication [20, 23].
- Excluding non-peer-reviewed data available only in abstracts, which did not enable critical appraisal [16–19].
- Obtaining confirmation from a lead author that two randomised studies conducted at the same centre were separate patient samples [13, 14].
- Determining whether the data from non-English-language papers [11, 25] were pivotal to the analyses (MTEP procedure is to include such data only when this criterion is met, and with translation by a proper agency), with translation of one paper into English [25].
- Correcting data entry errors.
- For outcomes expressed as RRs, excluding studies with zero events in both study arms, as this precluded RR calculation [11, 14, 25].
- Excluding from the meta-analyses one outlying study conducted in China, which generated heterogeneity for two outcomes (hospital stay and time to catheter removal), because the EAC considered that both outcomes are driven by local practice, which may differ between healthcare providers [13].

The results of the EAC's meta-analyses are summarised in Table 3, alongside those of the company.

The EAC analysis found that TURis significantly reduced the risk of TUR syndrome (RR 0.18 [95 % CI 0.05–0.62]) and suggested that one case of TUR syndrome was prevented for every 50 patients treated with TURis. The EAC found that the risk of blood transfusion was significantly reduced (RR 0.35 [95 % CI 0.19–0.65]), suggesting that one case of transfusion was prevented for every 20 patients treated with TURis. Like the company, the EAC found no statistically significant reduction in clot retention (RR 0.55 [95 % CI 0.26–1.15]) and virtually no difference in procedure time (mean difference −1.36 [95 % CI −3.70 to 0.98] min) or time to removal of the catheter (mean difference −0.09 [95 % CI −0.25 to 0.06] days). In contrast to the company's analysis, the EAC's analysis found no substantial reduction in the hospital stay through the use of TURis (mean difference −0.19 [95 % CI −0.46 to 0.07] days).

The remaining outcome measures specified in the scope were readmission for repeat procedures, healthcare-associated infection, quality of life and device-related adverse events.

The EAC performed a meta-analysis of the rate of repeat procedures due to incomplete resection (Table 3) and found no significant difference between TURis and mTURP (RR 0.76 [95 % CI 0.42–1.40]). The EAC also

Table 1 Randomised studies of transurethral resection in saline (TURis) versus monopolar transurethral resection of prostate (mTURP) included in the analysis by the External Assessment Centre (EAC)

Study	Country	Sample size	Follow-up	Method of random allocation	Concealed allocation	Blinded assessment of outcome	Comments
Akman [12]	Turkey	286 patients were enrolled; 257 were analysed for long-term outcomes TURis group: $n = 127$ mTURP group: $n = 130$	12 months	NR	NR	NR	
Chen (I) [13]	China	45 patients were enrolled; 40 were analysed TURis group: $n = 21$ mTURP group: $n = 19$	6 months	NR	NR	NR	The authors confirmed that this study was different from the Chen (II) study
Chen (II) [14]	China	100 patients were randomised and analysed TURis group: $n = 50$ mTURP group: $n = 50$	2 years	Permuted algorithm stratified for age, prostate volume and baseline symptom severity	NR	Investigators were not blinded to allocation, but patients were	The authors confirmed that this study was different from the Chen (I) study
Fagerstrom [6, 15]	Sweden	202 men were randomised; 185 were analysed TURis group: $n = 98$ mTURP group: $n = 87$	18 months	Random number table	NR	NR	The 2 papers report distinctly different outcome measures occurring at different follow-up points
Geavlete [34]	Romania	340 patients TURis group: $n = 170$ mTURP group: $n = 170$	18 months	NR	Sealed envelope	Yes: patients and assessors of outcome	Data used from 2 arms of a 3-arm study
Ho [35]	Singapore	100 men were randomised and analysed TURis group: $n = 48$ mTURP group: $n = 52$	12 months	Computer program	NR	NR	

Table 1 continued

Study	Country	Sample size	Follow-up	Method of random allocation	Concealed allocation	Blinded assessment of outcome	Comments
Michielsen [20–24]	Belgium	550 patients were randomised TURis group: $n = 285$ mTURP group: $n = 265$	32.1 months (mTURP) and 31.4 months (TURis), based on a subset of 263 TURis patients and 255 mTURP patients	NR	Sealed envelope	No	The data are published in 5 papers representing 3 reports at different stages of accrual and with significant overlap, i.e. 238 patients (January 2005 to June 2006), 518 patients (January 2005 to January 2009) and 550 patients (January 2005 to August 2009) plus 2 subgroup analyses for men with large prostate glands and men on anticoagulants
Rose [25]	Germany	128 patients in total: 56 were treated for bladder cancer and 72 were treated for BPE TURis group: $n = 38$ (prostate) mTURP group: $n = 34$ (prostate)	NR	NR	NR	NR	The EAC found the study to be pivotal to analysis of readmission due to haemorrhage, and obtained a translation into English. All data utilised are for patients with BPE (not those treated for bladder cancer)

BPE benign prostatic enlargement, *NR* not reported

Table 2 Randomised studies of transurethral resection in saline (TURis) versus monopolar transurethral resection of prostate (mTURP) excluded from the analysis by the External Assessment Centre (EAC)

Study	Country	Sample size	Follow-up	Comments
Abascal-Junquera [11]	Spain	45 men TURis group: $n = 24$ mTURP group: $n = 21$	NR	Spanish-language paper with English-language abstract; the data were not pivotal to any meta-analysis, so the data were excluded from the EAC report
Goh/Gulur [16–19]	NR	210 patients were recruited and randomised; the first 156 were followed up with IPSSs and flow rates TURis group: $n = 110$ (80 were followed up) mTURP group: $n = 100$ (76 were followed up)	12 months	Abstracts only; it is not clear for all outcomes whether they were based on the entire sample (210 patients) or only the 156 patients who were followed up for 12 months

IPSS International Prostate Symptom Score, *NR* not reported

undertook a meta-analysis of readmission due to haemorrhage (Table 3) and found little difference between the groups (RR 0.53 [95 % CI 0.22–1.25]).

The EAC recorded data on infection, where available from studies, and concluded that there was little difference in infection rates between TURis and mTURP. Likewise, studies that reported either quality of life or functional urological measures after treatment suggested that TURis and mTURP were equivalent [12–15, 29, 34].

Because of a concern over higher energy settings used in TURis, the EAC undertook meta-analyses of the longer-term complications of urethral stricture and bladder neck contracture, and found no difference in risk between TURis and mTURP (Table 3).

The company identified four adverse events from the US Food and Drug Administration's Manufacturer and User Facility Device Experience (MAUDE) database [37] and the Medicines and Healthcare Products Regulatory Agency (MHRA) database [38]. The EAC identified an additional 13 adverse events from the same sources, but these sources were prone to either duplication or under-reporting of events, and the EAC could not establish that every adverse event was related to TURis. The commonest adverse event was breakage or degeneration of the electrode. Other events were failure to coagulate, urethral burns, bladder rupture and air embolism leading to cardiac arrest. Adverse events should be considered in the context of those that arise during mTURP.

4.2 Economic Evidence

4.2.1 Company's Economic Submission

The company identified three economic studies [39–41], and the EAC identified one additional study, which included an economic estimation [36], but these were not used as evidence for TURis by the company or by the EAC, because of low applicability to the scope.

The company provided a de novo economic model in the form of a decision tree with an NHS perspective and 2013 prices. The model matched the scope in terms of the population (men with LUTS secondary to BPE in whom surgical intervention is indicated), intervention (TURis) and comparator (mTURP). Patients entering the model were treated either with TURis or with mTURP. The following complications were included in the base case: TUR syndrome and blood transfusion. The time horizon of the model was not defined, but it was designed to capture early surgical complications.

No capital cost for mTURP was included, since mTURP capital equipment was assumed to be already in place under standard care. For TURis capital costs, the model considered existing Olympus customers and non-Olympus customers independently, since new customers would require more new equipment, assumed to be three each of a telescope, light guide, inner sheath and outer sheath (total £26,715). Existing Olympus customers had some components already, so their capital cost was £8,800. The model did not consider the capital cost of the generator in any instance, because generators are supplied to customers free of charge as part of a contract to buy a volume of consumables. The company assumed that three sets of TURis capital equipment (excluding the generator) would suffice, enabling up to three TURis operations to be carried out per session, but no more, because the equipment needs to be cleaned before re-use. A discount rate of 3.5 % was applied to the capital equipment cost of TURis beyond the first year.

In addition to the base case, the company included three optional scenarios in the model:

1. Considering the cost of readmission due to clot retention.

Table 3 Summary of meta-analyses of randomised trials conducted by the company and by the External Assessment Centre (EAC)

Outcome measure	Company's included studies	Company's result	EAC's included studies	EAC's results
TUR syndrome	Abascal-Junquera [11] Akman [12] Chen (II) [14] Goh [17] Michielsen [21] Rose [25]	RR 0.28 (95 % CI 0.08–1.02) CI includes null value p = NS	Akman [12] Chen (I) [13] Fagerstrom [15] Geavlete [34] Ho [35] Michielsen [21]	Fixed-effects model: RR 0.18 (95 % CI 0.05–0.62) Overall effect: $p = 0.006$ Heterogeneity: $\chi^2 = 0.20$, $df = 5$, $p = 1.00$, $I^2 = 0$ % ARR = −0.02 (95 % CI −0.03 to −0.01) NNT = 50 (95 % CI 33–100)
Blood transfusion	Akman [12] Chen (II) [14] Fagerstrom [6]	RR 0.36 (95 % CI 0.16–0.80) No p value reported	Akman [12] Chen (I) [13] Chen (II) [14] Fagerstrom [6] Geavlete [34] Ho [35]	Fixed-effects model: RR 0.35 (95 % CI 0.19–0.65) Overall effect: $p = 0.0008$ Heterogeneity: $\chi^2 = 0.83$, $df = 5$, $p = 0.97$, $I^2 = 0$ % ARR = −0.05 (95 % CI −0.07 to −0.02) NNT = 20 (95 % CI 14–50)
Clot retention	Akman [12] Michielsen [20]	RR TURis/mTURP 0.63 (95 % CI 0.21–1.90) p = NS	Akman [12] Chen (II) [14] Geavlete [34] Ho [35] Michielsen [20]	Fixed-effects model: RR 0.55 (95 % CI 0.26–1.15) Overall effect: $p = 0.11$ Heterogeneity: $\chi^2 = 2.71$, $df = 4$, $p = 0.61$, $I^2 = 0$ %
Hospital stay	Akman [12] Chen (I) [13] Michielsen [23]	Mean difference −0.52 (95 % CI −0.74 to −0.30) days $p = 0.0001$	Akman [12] Michielsen [23]	Fixed-effects model: Mean difference −0.19 (95 % CI −0.46 to 0.07) days Overall effect: $p = 0.16$ Heterogeneity: $\chi^2 = 0.01$, $df = 1$, $p = 0.92$, $I^2 = 0$ %
Time to catheter removal	Akman [12] Chen (I) [13] Michielsen [23]	Mean difference −0.23 (95 % CI −0.38 to −0.08) days	Akman [12] Michielsen [23]	Fixed-effects model: Mean difference −0.09 (95 % CI −0.25 to 0.06) days Overall effect: $p = 0.24$ Heterogeneity: $\chi^2 = 1.08$, $df = 1$, $p = 0.30$, $I^2 = 8$ %
Procedure time	Akman [12] Chen (II) [14] Fagerstrom [6] Michielsen [23]	Mean difference −1.68 (95 % CI −4.18 to 0.81) minutes	Akman [12] Chen (II) [14] Fagerstrom [6] Ho [35] Michielsen [23]	Fixed-effects model: Mean difference −1.36 (95 % CI −3.70 to 0.98) minutes Overall effect: $p = 0.26$ Heterogeneity: $\chi^2 = 5.00$, $df = 4$, $p = 0.29$, $I^2 = 20$ %

Table 3 continued

Outcome measure	Company's included studies	Company's result	EAC's included studies	EAC's results
Readmission due to haemorrhage	NA	NA	Fagerstrom [15] Geavlete [34] Rose [25]	Fixed-effects model: RR 0.53 (95 % CI 0.22–1.25) Overall effect: $p = 0.15$ Heterogeneity: $\chi^2 = 4.26$, $df = 2$, $p = 0.12$, $I^2 = 53$ % ARR = −0.04 (95 % CI −0.07 to −0.01) NNT = 25 (95 % CI 14–100)
Urethral stricture/bladder neck contracture (aggregated outcome)	NA	NA	Akman [12] Chen (II) [14] Fagerstrom [15] Geavlete [34] Ho [35] Michielsen [24]	Fixed-effects model: RR 1.08 (95 % CI 0.70–1.69) Overall effect: $p = 0.72$ Heterogeneity: $\chi^2 = 3.10$, $df = 5$, $p = 0.69$, $I^2 = 0$ %
Urethral stricture	NA	NA	Chen (II) [14] Fagerstrom [15] Geavlete [34] Ho [35] Michielsen [23]	Fixed-effects model: RR 1.09 (95 % CI 0.60–1.97) Overall effect: $p = 0.77$ Heterogeneity: $\chi^2 = 2.12$, $df = 4$, $p = 0.71$, $I^2 = 0$ %
Bladder neck contracture	NA	NA	Chen (II) [14] Fagerstrom [15] Geavlete [34]	Fixed-effects model: RR 0.88 (95 % CI 0.35–2.20) Overall effect: $p = 0.79$ Heterogeneity: $\chi^2 = 0.69$, $df = 2$, $p = 0.71$, $I^2 = 0$ %
Repeat procedure due to incomplete resection	NA	NA	Fagerstrom [15] Geavlete [34] Michielsen [20]	Fixed-effects model: RR 0.76 (95 % CI 0.42–1.40) Overall effect: $p = 0.38$ Heterogeneity: $\chi^2 = 3.59$, $df = 2$, $p = 0.17$, $I^2 = 44$ %

ARR absolute risk reduction (TURis minus mTURP), *CI* confidence interval, *df* degrees of freedom, *mTURP* monopolar transurethral resection of prostate, *NA* not applicable, *NNT* number needed to treat, *NS* nonsignificant, *RR* relative risk (TURis/mTURP), *TUR* transurethral resection, *TURis* transurethral resection in saline

2. Including re-operations due to the initial procedure being terminated prior to completion.
3. Assuming that TURis reduces the hospital stay by 1 day in comparison with mTURP.

The base case inputs for the model were drawn from several sources. Clinical parameters were drawn from the company's meta-analysis. The difference in hospital stay between TURis and mTURP was taken from the company's meta-analysis, but the mean length of stay for mTURP was taken from hospital episode statistics (HES) data for 2012–2013 [42]. The additional resources required for treating patients with TUR syndrome, as used by the company, were based on a 2-day stay in a high-dependency unit, followed by a 2-day stay in a general ward, utilising the national schedule of reference costs for 2012–2013 [43, 44]. The resources required for a blood transfusion in the company's model were taken from a published study [45]. The cost of re-operation due to the initial procedure being terminated prior to completion was calculated in the company's model as the cost of consumables plus the cost of the hospital stay.

The company's base case analysis showed that TURis is cost saving in comparison with mTURP. For existing Olympus customers, the saving per case was £133.63, and for non-Olympus customers, it was £114.19. The company conducted one-way deterministic sensitivity analysis for ten input variables and found that TURis remained cost saving across the range of values tested. The company also performed probabilistic sensitivity analysis, whereby each model parameter was assigned a statistical distribution and the model was run for 1000 simulations, by randomly sampling the distributions and calculating the results of the model each time. TURis remained cost saving in almost all of the simulations.

4.2.2 *Critique of Economic Evidence*

The key drivers of the company's model were the reduction in the hospital stay for TURis patients in comparison with mTURP, the cost of a bed-day and the cost of mTURP consumables. The reduction in the hospital stay of 0.52 days was based on the company's meta-analysis, in which a single study [13] introduced heterogeneity into the data. After removing this study, the EAC found a difference in the hospital stay of 0.19 days ($p = 0.16$) and considered this difference to be small in magnitude and not statistically significant. However the committee considered that the point estimate of a reduction in the hospital stay of 0.19 days should be used in the model.

The cost of mTURP consumables was estimated by the company to be 50 % of the cost of TURis consumables (£80.57 per case). The EAC considered that for a key driver of the model, it is more appropriate to use an accurate cost where this is available.

The EAC considered that the company had overestimated the cost of blood transfusion, by including several blood products (red blood cells, plasma, platelets and cryoprecipitate). Clinical advisers confirmed that the EAC proposal of 2.7 units of red blood cells alone was a reasonable estimate for transfusion for mTURP patients.

The EAC considered that the company's model did not consider the case where non-Olympus customers perform mTURP with their own capital equipment but sourcing cheaper mTURP consumables independently via NHS Supply Chain. The EAC modified the model to explore this scenario.

4.2.3 *External Assessment Centre's Revisions of the Company's Economic Model*

The four most significant modifications made to the company's model by the EAC were:

1. Changing the cost of mTURP consumables in the base case.
2. Changing the reduction in hospital stay in the base case.
3. Changing the cost of blood transfusion in the base case.
4. Modelling an additional scenario based on limited evidence [15] of a reduction in readmission (due to any cause) following TURis.

These are explained as follows. For existing Olympus customers, the EAC changed the cost of mTURP consumables from £80.57 to £137.75 per case on the basis of Olympus price list prices. For non-Olympus customers independently sourcing consumables for mTURP, the consumables cost per case was changed from £80.57 to £56.84 on the basis of NHS Supply Chain prices. Clinical experts confirmed that this was realistic. The EAC changed the reduction in the hospital stay in favour of TURis from 0.52 days to 0.19 days on the basis of its own meta-analysis (Table 3) and at the request of the committee. The EAC changed the cost of blood transfusion from £920.40 to £329 to reflect the cost of 2.7 units of packed red cells [45].

On the basis of its own meta-analyses, the EAC also made minor modifications to the risk of TUR syndrome in mTURP cases and the likelihood of blood transfusion (Table 3).

On this basis, the EAC base case analysis found TURis to be cost saving at £70.55 per case for Olympus customers and cost incurring at £19.80 per case for non-Olympus customers.

The EAC's additional scenario considered the only available randomised trial [15] that reported rates of

readmission (due to any cause) following TURis (5.1 %) and mTURP (16.1 %). The platform for this analysis was the company's scenario of readmission due to clot retention, and the EAC used the company's estimated cost of readmission of £2781, based on an NHS reference cost for admission with urological complications [43]. There is uncertainty regarding this cost, which may not be accurate for all causes of readmission. The effect on the EAC's base case was that TURis was strongly cost saving by £375.02 per case for Olympus customers and £284.66 per case for non-Olympus customers. This result must be treated with caution because of the uncertainty of the modelled cost and because the rates of readmission due to any cause were based on just one randomised trial [15] and were not reported in the other randomised trials [12–14, 20–25, 34, 35].

5 NICE Guidance

5.1 Preliminary Guidance

The evidence submitted by the company and the EAC's report were presented to the Medical Technologies Advisory Committee (MTAC), who produced the following draft recommendations:

"The case for adopting the transurethral resection in saline (TURis) system for resection of the prostate is supported by the evidence. Using bipolar diathermy with TURis instead of a monopolar system avoids the risk of transurethral resection syndrome and reduces the need for blood transfusion. It may also reduce the length of hospital stay and hospital readmissions".

"Using the transurethral resection in saline (TURis) system instead of monopolar transurethral resection of the prostate (TURP) results in an estimated saving of £71 per patient for hospitals that already use an Olympus monopolar system and an estimated additional cost of £20 per patient for other hospitals. The savings are driven by reductions in length of hospital stay and consumable costs. However, there is some evidence of a reduction in readmissions with the TURis system compared with monopolar TURP. If this evidence is included, using the TURis system results in an estimated saving of £375 per patient for hospitals that already use an Olympus monopolar system and an estimated saving of £285 per patient for other hospitals."

5.2 Consultation Response

During the consultation period, NICE received 12 consultation comments from four consultees (one manufacturer, one External Assessment Centre, one specialist society and one patient organisation). The comments concerned terminology, numerical errors and whether TURis raised new concerns in comparison with mTURP in three areas: the incidence of dysuria following surgery, training requirements for surgical teams and equity of access to surgery for all men covered by the scope [8]. The committee's responses provided reassurance that TURis did not impose a substantial training requirement for surgical teams and that equity issues were given full consideration in the guidance. Four urologist expert advisors confirmed to the committee that the incidence of dysuria was similar following TURis and mTURP. There were therefore few changes made in preparation of the final NICE guidance on TURis.

6 Key Challenges and Learning Points

In contrast to many medical technologies, there was a relatively large quantity of good-quality evidence for the TURis technology. However, heterogeneity in the data led to differences in interpretation. None of the studies were from the UK, and differences in procedural measures, such as the length of the hospital stay, may depend on local practices.

In the UK, there are a number of procurement routes for medical technologies: buying the device outright, leasing the device and receiving the device free of charge as part of an arrangement to purchase an agreed number of consumables. If the device is purchased outright, the hospital may choose to purchase suitable third-party consumables. In addition, upgrading to a new system for performing a given procedure may allow utilisation of compatible capital equipment already in place if the hospital stays with the existing provider. This saving would need to be considered against whether the provider's new system conveyed advantages over similar systems from competitor providers. This assessment demonstrated that each of these issues can have an important impact on the resource consequences of adopting the new technology.

7 Conclusion

The evidence from eight randomised trials [6, 12–15, 20–25, 34, 35] demonstrates that the efficacy of TURis is equivalent to that of mTURP in terms of improving LUTS due to BPE and is associated with a reduced risk of TUR syndrome and reduced need for blood transfusion in comparison with mTURP. The clinical data are uncertain as to whether TURis shortens the hospital stay.

The NICE guidance supports the adoption of the TURis technology for performing TURP in men with LUTS due to BPE [3].

Following critical appraisal and appropriate revisions to the company's base case economic analysis, TURis was cost saving by £70.55 per case for existing Olympus customers and cost incurring by £19.80 per case for non-Olympus customers.

If data from a single randomised study [15], suggesting that rates of readmission (due to any cause) are lower for TURis than for mTURP, are repeatable in practice, then TURis is strongly cost saving irrespective of the likely purchasing arrangement in place. There is uncertainty in this finding, as it is based on a single study [15], and further data from randomised studies that measure any-cause readmission would be useful.

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Compliance with Ethical Standards

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